Oral isotretinoin and pregnancy prevention programmes

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Oral isotretinoin has had a major positive impact on the lives of countless patients since its introduction in the early 1980s. Of course, we feel it is imperative to provide oral isotretinoin to our patients in the safest manner possible. But we also believe that instituting increasingly restrictive programmes around the use of the drug may not be the optimal approach in view of the limitations of such programmes. In particular, restrictive programmes such as iPLEDGE may have reached the limit of influencing human behaviour. More restrictive programmes, apart from mandated use of injectable long-acting contraceptives, cannot prevent unintended pregnancies resulting from failure to use contraceptives appropriately. We think that the situation is similar for Europe. Until there are improved options for the patients who are now isotretinoin candidates, it is important to take a balanced approach that allows for appropriate use of this important drug. We are saddened that the article by Shin *et al.* suggests that women selectively may be receiving fewer prescriptions for isotretinoin, despite the fact that prescription levels for males have remained relatively constant. We agree with a recent editorial by Maloney and Stone[15] suggesting that a team or committee evaluation of prescribing patterns and fetal exposure would be a valuable addition to the current system with the goal of improving patient access and outcomes.

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Oral isotretinoin and pregnancy prevention programmes: reply from authors

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Madam, We thank Professors Thiboutot, Gollnick, Bettoli, Dréno, Kang, Leyden, Shalita and Torres[1] for the Global Alliance to Improve Outcome in Acne, for their comments on our article.[2] Their letter points out an important aspect of having acne and the effectiveness of isotretinoin in treating this disorder.

Thiboutot *et al.* draw attention to the effectiveness of isotretinoin and the psychological burden of acne. Most patients with acne are in the age group of 12–20 years and approximately 50% are females of childbearing potential.

The effectiveness of isotretinoin was not considered the subject of discussion in our paper. We agree that the effectiveness of isotretinoin is well acknowledged[3] and the benefit–risk balance is considered to be positive, provided that the pregnancy prevention programme (PPP) is adhered to.

The major concern for isotretinoin is its teratogenicity.

The risk of congenital anomalies with isotretinoin should be minimized in a way such that it can still be prescribed for the treatment of acne with the least restraints. This can only be achieved when both healthcare professionals and patients are aware of – and are compliant with – the PPP. By creating awareness of noncompliance with the PPP, it is hoped that prescribers, pharmacists and patients will adjust their routine and take responsibility for adhering to the PPP.

The iPLEDGE programme in the U.S.A. contains a PPP with stricter rules and requirements compared with the previous programme 'System to Manage Accutane-Related Teratogenicity' (SMART). Research showed that iPLEDGE did not decrease the pregnancy rate[4] compared with the rate while SMART was in place. This information might suggest that other actions might be necessary to improve the prevention of pregnancies and the adherence to the programme.

We agree with Thiboutot *et al.* that the emotional aspect of acne should not be trivialized; however, the retinoid embryopathy might also have a major impact, as well as the emotional burden of induced or spontaneous abortion in patients getting pregnant while using isotretinoin. Based on the current experience with the programmes (PPPs), we also would like to support the suggestion of Maloney and Stone[5] to develop a multidisciplinary team that will review all available data to detect where the system fails and where it over-regulates. Our joint aim is to keep an effective treatment for acne on the market while causing the least restraints but with a high compliance for measures to minimize the risk of congenital anomalies due to isotretinoin.

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